Title:

Other race effect on amygdala response during affective facial processing in major depression

Running head:

Other race effect on amygdala response in depression

Authors:

Anjali Sankar[1], Sergi G. Costafreda[2], Lauren B. Marangell[3], Cynthia H.Y. Fu [4,5]

1. Department of Psychiatry, Stony Brook University, Stony Brook, NY11794, USA
2. Division of Psychiatry, Faculty of Brain Sciences, University College London, London, UK
3. University of Texas Health Science Center, Houston, USA
4. Centre for Affective Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
5. School of Psychology, University of East London, London, UK

Corresponding author:

Anjali Sankar, Department of Psychiatry, Health Sciences Center T-10, Stony Brook University, Stony Brook, NY11794, USA

Email: anjali.sankar@stonybrookmedicine.edu

Abstract

Objective: The other race effect, also known as own race bias, refers to the enhanced ability to recognize faces belonging to one's own race relative to faces from another race. The other race effect is associated with increased amygdala response in healthy individuals. The amygdala is a key node in emotion processing which shows impaired functioning in depression and has been proposed to be a marker of depressive state. We investigated the impact of the other race effect on amygdala responses in depression.

Methods: Participants were 30 individuals with major depression (mean age39.4 years) and 23 healthy individuals (mean age: 38.8 years) recruited from the community. Participants were Asian, Black/African American and Caucasian. During a functional MRI scan, participants viewed Caucasian faces which displayed a range of sad expressions. A region of interest analysis of left and right amygdala responses was performed.

Results: Increased bilateral amygdala responses were observed in response to the Caucasian face stimuli in participants who were Asian or Black/African American as compared to Caucasian participants in both healthy individuals and individuals with major depression. There was no significant group by race interaction effect.

Conclusions: Increased amygdala responses associated with the other race effect were evident in both individuals with major depression and in healthy participants. Increased amygdala responses with the other race effect is a potential confound of the neural correlates of facial processing in healthy participants and in mental health disorders. The implications of the other race effect on impairments in interpersonal functioning in depression require further investigation.

Key words

functional MRI, BOLD, neural correlates, ORE, major depressive disorder

Introduction

The other race effect, also known as own race bias, describes the phenomenon of stronger recognition of faces to one's own race as compared to another race. While race and ethnicity are often used interchangeably, race generally refers to physical features and is associated with biology while ethnicity is associated with cultural factors such as language and customs. The other race effect has been demonstrated in healthy individuals amongst different races[25], is evident in infants[22, 23], and has been attributed to reduced exposure to other races or motivation to individuate faces of other races [33].

Greater amygdala activation has been linked with the other race effect in healthy individuals [8, 17, 27]. The amygdala is engaged by highly salient stimuli and is a key node in emotion processing, notably in the discernment of emotional facial expressions and in particular for negative expressions[6, 7, 30].An increased amygdala response to sad facial expressions is a widely replicated finding in major depression and has been proposed to be a marker of a current depressive state[2, 14, 15, 31].

However, if the other race effect is present in major depression and in turn engages the amygdala during facial processing, then the effect becomes a source of variance and is a potential confound in amygdala responses to emotional facial expressions. On the other hand, if increased amygdala activation reflects engagement primarily to the emotional expression, rather than to other aspects of facial processing including race, then the effect would not be observed.

Behavioural evidence of the other race effect in mental health disorders has been reported in schizophrenia and autism, both disorders are associated with pervasive deficits in processing facial expressions[28, 35].However, the effect has not been examined in major depression, only in healthy individuals who had undergone a sad mood induction, in which the other race effect was not observed regardless of the emotional facial expression[20]. The findings were understood as due to participants scanning and noting more features of the face during sad

mood induction, which suggest that the other race effect would not be expected in major depression.

We sought to examine the other race effect on amygdala responsivity to sad facial expressions in major depression. We applied a region of interest analysis to the amygdala given the findings of increased amygdala activation associated with the other race effect in healthy individuals[8, 17, 27] and the specificity of amygdala responses to sad facial expressions in major depression[2, 14, 15, 31]. The stimuli were standardized Ekman faces[11], a widely used set of facial expressions which are restricted to faces of Caucasian adults. We expected to observe the other race effect in healthy participants with increased amygdala activation, but whether the effect would be evident in major depression was less clear.

Material and Methods

The study was approved by the Cambridgeshire 4 NHS Research Ethics Committee, NHS Health Research Authority, and all participants had provided informed written consent. Participants were 30 individuals with major depression(mean age 39.4 years) and 23 healthy individuals (mean age 38.8 years)recruited from the community (Table 1). Participants were self-identified as Caucasian, Asian or African American, and there were no differences in age or gender between patients with depression and heathy controls (all $p>0.05$), or in age ($p=0.48$), gender ($p=0.25$) or depressive severity ($p=0.61$) between the Caucasian and the Asian/African American participants. None of the participants with major depression were taking antidepressant medication or had been in psychotherapy treatment for a minimum of 4 weeks. Healthy participants had no history of psychiatric illnesses. Full inclusion and exclusion criteria are described in Fu et al.[13].

During the functional MRI scan, participants viewed a series of 10 faces (5 female), all Caucasian, adapted from Ekman and Friesen's Pictures of Facial Affect [11]and morphed using a computer program to depict varying intensities of sadness: low, medium and high[14]. During

the task, participants were required to indicate the gender of the face by a button press such that the explicit instruction was gender identification which facilitated implicit processing of the emotion [14].The facial stimuli were presented twice at each intensity (60 faces in total), along with 12 baseline trials consisting of a crosshair visual fixation point, for a total of 72 presentations, in a pseudo-randomised order. Each stimulus was presented for a duration of 3 seconds, and the interval between trials varied randomly according to a Poisson distribution, with a mean intertrial interval of 5 seconds, for a total duration of 360 seconds (6 minutes).

Gradient echo T2*-weighted echoplanar images were acquired depicting blood oxygenation level-dependent (BOLD) contrast. A total of 180 volumes were acquired for the sad facial affect task. For each volume, 39 oblique axial slices parallel to the intercommissural plane were collected with the following parameters: slice thickness: 3 mm, slice gap: 0.3 mm, echo time (TE): 30 milliseconds, repetition time (TR): 2000 milliseconds, flip angle: 75°, field of view: 240 mm, and matrix size: 64 x 64.

The left and right amygdala regions of interest were defined according to the Harvard-Oxford probability atlas distributed with the FSL package (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases).Statistical Parametric Mapping (SPM8, Wellcome Department of Imaging Neuroscience, London, UK: http://www.fil.ion.ucl.ac.uk/spm) was used to pre-process and analyse the task-related fMRI data. The images were realigned to correct for motion artefacts, spatially normalized to the Montreal Neurological Institute (MNI) template, and smoothed using an 8mm full-width at half maximum (FWHM) Gaussian kernel filter. First-level analysis was performed using the general linear model, accounting for serial autocorrelations by applying an autoregressive model. Stimuli presentation was modelled as individual events and the first level analysis produced contrast images depicting overall facial processing capacity (mean difference in response between all facial trials taken together and baseline trials)[14]. Region of interest analysis was performed using the MarsBar tool in SPM8

(http://marsbar.sourceforge.net/). The BOLD responses for left and right amygdalae were extracted separately for each subject in the contrast of interest. A multivariate analysis of variance (MANOVA)was performed for left and right amygdala separately using the extracted values with ethnicity as the between group measure (Caucasian, non-Caucasian).

Results

There was a significant effect of race on amygdala activation ($F_{2,48}$=5.025, p=0.010) (Figure 1), in which the subsequent univariate analysis showed a statistically significant difference between Caucasian and non-Caucasian participants in both right ($F_{1,49}$=10.23, p=0.002) and left ($F_{1,49}$=5.13,p=0.028) amygdala responses to sad facial expressions. Non-Caucasian participants showed greater right (t_{51}= 2.87, p=0.006) and left (t_{51}= 2.17, p=0.035) amygdala activation relative to Caucasian participants. The multivariate tests did not reveal any significant effects of group ($F_{2,48}$=2.54, p=0.089) or any significant group by race interactions ($F_{2,48}$=0.935, p=0.400) on amygdala responses.

There were no correlations between depression severity and amygdala response in Caucasian (n=17; right amygdala: p=0.72; left amygdala: p=0.91) or non-Caucasian participants with depression (n=13; right amygdala: p=0.49; left amygdala: p=0.45).

Discussion

The present findings highlight the strength of engagement of the amygdala associated with the other race effect irrespective of depression status. Both healthy participants and those with major depression who were Asian and African American demonstrated increased bilateral amygdala responses to sad expressions in Caucasian faces in comparison with Caucasian participants. The lack of a significant group by race interaction effect indicates that there were comparable effects in healthy participants and in individuals with depression.

Moreover, we did not find a relationship between depression severity and amygdala response in Caucasian or non-Caucasian participants with depression. Whether there could be dissociable effects in individuals with depression, in which those with greater depressive severity would demonstrate sustained engagement to sad facial expressions that is above the contribution of the other race effect, should be ascertained in a larger sample.

While the other race effect has been well established in healthy individuals, there have been few studies in mental health disorders. Reports in schizophrenia [28] and in autism [35] have found a significant other race effect for emotion recognition and face memory. Moreover, participants with autism demonstrated similar cross-racial differentiation methods in scanning faces to that observed in healthy individuals [35]. The effect though has not been examined in major depression, while findings in healthy individuals following a sad mood induction did not observe a significant other race effect which was understood as a sad mood being associated with more detailed facial scan patterns that reduce susceptibility to the other race effect[20]. However, the present findings indicate that the other race effect is evident in major depression, in contrast to the findings from the mood induction in healthy participants. How the effect relates to patterns in facial sampling though would benefit from eye-tracking measures in participants with major depression.

Investigations of neural mechanisms of the other race effect have largely been examined using event related brain potential (ERP) studies and in healthy individuals. In particular, the early N170 component is purported to be involved in the processing of global facial features and less likely to be modulated by individual facial parts[9, 10]. Findings have been inconsistent though with the N170 component showing little sensitivity to the race of the facial stimuli [4, 5, 18, 34] as well as higher N170 responses to one's in-group [29] or to other race group[19, 21]. Modulation of N170 responses [26]by attentional demand could have contributed to the variation in responses, and impact of the other race effect may emerge in later epochs as the N200 and

N400 components have revealed differences in processing own versus other-race faces (see[32] for a review).

Functional MRI studies have revealed recruitment within the network involved in face processing including in the amygdala[8, 17, 27], which is engaged by salient emotional and social stimuli, and the fusiform cortex, a region highly specialized for face processing which shows greater activation during recognition [16, 24] and categorization [12] of faces from own- relative to another race. Intentional encoding of same- and other-race faces could be further modulated by frontoparietal networks subserving attention and cognitive control [3].Factors which moderate the other race effect include external factors, such as familiarity of the face, as the effect on amygdala [8, 27] and fusiform [24] activations is no longer evident when the face is that of a well-known (famous) individual[24, 27], and the duration of the stimuli presentation, as the effect is not observed with extended presentations [8],suggesting that the novelty or the unfamiliarity of the faces contribute to the bias-related responses. Moreover, it is possible that the effect could be modulated by the degree of implicit racial bias for a particular individual.

In the present study, we had sought to focus on amygdala activation and we used sad facial expressions as the stimuli because of their particular salience in major depression [30]. Whether the other race effect would be observed with other emotional face expressions requires further investigation. As the facial stimuli were all Caucasian, we were not able to confirm whether the other race effect would be found for Caucasian participants with depression viewing non-Caucasian faces.

Conclusion

In conclusion, increased amygdala activation was associated with the other race effect in both healthy participants and in individuals with major depression. The amygdala has a key role in emotion processing, social cognition and in the regulation of social behavior[1]. The potential

191 interaction of these effects and the implications for the impairments in social interactions that
192 are already evident in depression require further investigation.

References

[1] R. Adolphs, COGNITIVE NEUROSCIENCE OF HUMAN SOCIAL BEHAVIOUR, NATURE REVIEWS| NEUROSCIENCE 4 (2003) 165.

[2] D. Arnone, S. McKie, R. Elliott, E.J. Thomas, D. Downey, G. Juhasz, S.R. Williams, J.W. Deakin, I.M. Anderson, Increased amygdala responses to sad but not fearful faces in major depression: relation to mood state and pharmacological treatment, American Journal of Psychiatry 169 (2012) 841-850.

[3] T.I. Brown, M.R. Uncapher, T.E. Chow, J.L. Eberhardt, A.D. Wagner, Cognitive control, attention, and the other race effect in memory, PloS one 12 (2017) e0173579.

[4] R. Caldara, B. Rossion, P. Bovet, C.-A. Hauert, Event-related potentials and time course of the 'other-race'face classification advantage, Neuroreport 15 (2004) 905-910.

[5] R. Caldara, G. Thutb, P. Servoir, C. Michel, P. Bovet, B. Renault, Face versus non-face object perception and the 'other-race'effect: a spatio-temporal event-related potential study, Clinical Neurophysiology 114 (2003) 515-528.

[6] S.G. Costafreda, M.J. Brammer, A.S. David, C.H. Fu, Predictors of amygdala activation during the processing of emotional stimuli: a meta-analysis of 385 PET and fMRI studies, Brain research reviews 58 (2008) 57-70.

[7] S.G. Costafreda, P. McCann, P. Saker, J.H. Cole, S. Cohen-Woods, A.E. Farmer, K.J. Aitchison, P. McGuffin, C.H. Fu, Modulation of amygdala response and connectivity in depression by serotonin transporter polymorphism and diagnosis, Journal of affective disorders 150 (2013) 96-103.

[8] W.A. Cunningham, M.K. Johnson, C.L. Raye, J.C. Gatenby, J.C. Gore, M.R. Banaji, Separable neural components in the processing of black and white faces, Psychological Science 15 (2004) 806-813.

[9] M. Eimer, Event-related brain potentials distinguish processing stages involved in face perception and recognition, Clinical neurophysiology 111 (2000) 694-705.

[10] M. Eimer, A. Gosling, S. Nicholas, M. Kiss, The N170 component and its links to configural face processing: a rapid neural adaptation study, Brain research 1376 (2011) 76-87.

[11] P. Ekman, W. Friesen, Pictures of Facial Affect (Palo Alto, CA: Consulting Psychologists), (1976).

[12] L. Feng, J. Liu, Z. Wang, J. Li, L. Li, L. Ge, J. Tian, K. Lee, The other face of the other-race effect: An fMRI investigation of the other-race face categorization advantage, Neuropsychologia 49 (2011) 3739-3749.

[13] C.H. Fu, S.G. Costafreda, A. Sankar, T.M. Adams, M.M. Rasenick, P. Liu, R. Donati, L.A. Maglanoc, P. Horton, L.B. Marangell, Multimodal functional and structural neuroimaging investigation of major depressive disorder following treatment with duloxetine, BMC psychiatry 15 (2015) 82.

[14] C.H. Fu, S.C. Williams, A.J. Cleare, M.J. Brammer, N.D. Walsh, J. Kim, C.M. Andrew, E.M. Pich, P.M. Williams, L.J. Reed, Attenuation of the neural response to sad faces in major depressionby antidepressant treatment: a prospective, event-related functional magnetic resonance imagingstudy, Archives of general psychiatry 61 (2004) 877-889.

[15] C.H. Fu, S.C. Williams, A.J. Cleare, J. Scott, M.T. Mitterschiffthaler, N.D. Walsh, C. Donaldson, J. Suckling, C. Andrew, H. Steiner, Neural responses to sad facial expressions in major depression following cognitive behavioral therapy, Biological psychiatry 64 (2008) 505-512.

[16] A.J. Golby, J.D. Gabrieli, J.Y. Chiao, J.L. Eberhardt, Differential responses in the fusiform region to same-race and other-race faces, Nature neuroscience 4 (2001) 845-850.

[17] A.J. Hart, P.J. Whalen, L.M. Shin, S.C. McInerney, H. Fischer, S.L. Rauch, Differential response in the human amygdala to racial outgroup vs ingroup face stimuli, Neuroreport 11 (2000) 2351-2354.

[18] Y. He, M.K. Johnson, J.F. Dovidio, G. McCarthy, The relation between race-related implicit associations and scalp-recorded neural activity evoked by faces from different races, Social Neuroscience 4 (2009) 426-442.

[19] M. Herrmann, T. Schreppel, D. Jäger, S. Koehler, A.-C. Ehlis, A. Fallgatter, The other-race effect for face perception: an event-related potential study, Journal of neural transmission 114 (2007) 951-957.

[20] P.J. Hills, Z. Marquardt, I. Young, I. Goodenough, Explaining Sad People's Memory Advantage for Faces, Frontiers in psychology 8 (2017).

[21] T.A. Ito, G.R. Urland, The influence of processing objectives on the perception of faces: An ERP study of race and gender perception, Cognitive, Affective, & Behavioral Neuroscience 1 (2005) 21-36.

[22] D.J. Kelly, S. Liu, K. Lee, P.C. Quinn, O. Pascalis, A.M. Slater, L. Ge, Development of the other-race effect during infancy: Evidence toward universality?, Journal of experimental child psychology 104 (2009) 105-114.

[23] D.J. Kelly, P.C. Quinn, A.M. Slater, K. Lee, L. Ge, O. Pascalis, The other-race effect develops during infancy: Evidence of perceptual narrowing, Psychological Science 18 (2007) 1084-1089.

[24] J.S. Kim, H.W. Yoon, B.S. Kim, S.S. Jeun, S.L. Jung, B.Y. Choe, Racial distinction of the unknown facial identity recognition mechanism by event-related fMRI, Neuroscience letters 397 (2006) 279-284.

[25] C.A. Meissner, J.C. Brigham, Thirty years of investigating the own-race bias in memory for faces: A meta-analytic review. American Psychological Association, 2001.

[26] T.N. Mohamed, M.F. Neumann, S.R. Schweinberger, Perceptual load manipulation reveals sensitivity of the face-selective N170 to attention, Neuroreport 20 (2009) 782-787.

[27] E.A. Phelps, K.J. O'Connor, W.A. Cunningham, E.S. Funayama, J.C. Gatenby, J.C. Gore, M.R. Banaji, Performance on indirect measures of race evaluation predicts amygdala activation, Journal of cognitive neuroscience 12 (2000) 729-738.

[28] A.E. Pinkham, N.J. Sasson, M.E. Calkins, J. Richard, P. Hughett, R.E. Gur, R.C. Gur, The other-race effect in face processing among African American and Caucasian individuals with schizophrenia, American Journal of Psychiatry 165 (2008) 639-645.

[29] K.G. Ratner, D.M. Amodio, Seeing “us vs. them”: Minimal group effects on the neural encoding of faces, Journal of Experimental Social Psychology 49 (2013) 298-301.

[30] A. Sankar, C. Fu, Psychotherapy and antidepressant treatment effects on the functional neuroanatomy of depression Psychopathology Review 3 (2016) 16-28.

[31] S. Surguladze, M.J. Brammer, P. Keedwell, V. Giampietro, A.W. Young, M.J. Travis, S.C. Williams, M.L. Phillips, A differential pattern of neural response toward sad versus happy facial expressions in major depressive disorder, Biological psychiatry 57 (2005) 201-209.

[32] J.W. Tanaka, L.J. Pierce, The neural plasticity of other-race face recognition, Cognitive, Affective, & Behavioral Neuroscience 1 (2009) 122-131.

[33] L. Wan, K. Crookes, K.J. Reynolds, J.L. Irons, E. McKone, A cultural setting where the other-race effect on face recognition has no social–motivational component and derives entirely from lifetime perceptual experience, Cognition 144 (2015) 91-115.

[34] H. Wiese, J. Stahl, S.R. Schweinberger, Configural processing of other-race faces is delayed but not decreased, Biological psychology 81 (2009) 103-109.

[35] L. Yi, P.C. Quinn, C. Feng, J. Li, H. Ding, K. Lee, Do individuals with autism spectrum disorder process own-and other-race faces differently?, Vision research 107 (2015) 124-132.